

CLAIMS

What is claimed is:

1. A method of treating pain in a subject comprising administering to the subject a
5 therapeutically effective amount of a neutralizing, high affinity TNF α antibody, such
that said pain is treated.
2. The method of claim 1, wherein the antibody is an isolated human antibody, or
an antigen-binding portion thereof, that dissociates from human TNF α with a K_D of 1×10^{-8} M or less and a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, both determined by
10 surface plasmon resonance, and neutralizes human TNF α cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.
3. The method of claim 1, wherein the antibody is an isolated human antibody, or
15 an antigen-binding portion thereof with the following characteristics:
 - a) dissociates from human TNF α with a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or
less, as determined by surface plasmon resonance;
 - b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ
ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1,
20 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6,
7, 8 and/or 9;
 - c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ
ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2,
3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at
25 positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.
4. The method of claim 1, wherein the antibody is an isolated human antibody, or
an antigen-binding portion thereof, with a light chain variable region (LCVR)
comprising the amino acid sequence of SEQ ID NO:1 and a heavy chain variable region
30 (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.
5. The method of any one of claims 1, 2, 3, or 4, wherein the antibody is D2E7.

6. The method of any one of claims 1, 2, 3, or 4, wherein the pain is neuropathic pain.

5 7. A method for treating a subject suffering from pain, comprising administering to the subject an antibody, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNF α with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, both determined by surface plasmon resonance, and neutralizes human TNF α cytotoxicity in a standard *in vitro*
10 L929 assay with an IC_{50} of 1×10^{-7} M or less, such that the pain is treated.

8. A method for treating a subject suffering from pain, comprising administering to the subject an antibody such that the pain is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof with the following
15 characteristics:

a) dissociates from human TNF α with a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1,
20 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at
25 positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that the pain is treated.

9. A method for treating a subject suffering from pain in which TNF α activity is detrimental, comprising administering to the subject an antibody such that the pain is treated, wherein the antibody is an isolated human antibody, or an antigen-binding
30 portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that the pain is treated.

10. The method of any one of claims 7, 8, or 9, wherein the antibody is D2E7.
11. The method of any one of claims 7, 8, or 9, wherein the pain is neuropathic pain.
- 5 12. A method for treating a subject suffering from pain in which $\text{TNF}\alpha$ activity is detrimental, comprising administering to the subject D2E7 such that the pain is treated.
13. The method of claim 12, wherein the pain is neuropathic pain.
- 10 14. A method of treating neuropathic pain comprising administering to a subject suffering from neuropathic pain a therapeutically affective amount of an antibody, or an antigen-binding portion thereof, that dissociates from human $\text{TNF}\alpha$ with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, both determined by surface
- 15 plasmon resonance, and neutralizes human $\text{TNF}\alpha$ cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less, such that the neuropathic pain is treated.
15. The method of claim 14, wherein the antibody is D2E7.
- 20 16. A method for treating neuropathic pain comprising administering to a subject suffering from neuropathic pain an effective amount of D2E7.
17. A kit comprising:
- 25 a) a pharmaceutical composition comprising a $\text{TNF}\alpha$ antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier; and
- b) instructions for administering to a subject the $\text{TNF}\alpha$ antibody pharmaceutical composition for treating a subject who is suffering from pain.
18. A kit according to claim 17, wherein the $\text{TNF}\alpha$ antibody, or an antigen binding
- 30 portion thereof, is D2E7